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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/762,154
Filing Date: January 21, 2004
Appellant(s): NEZU ET AL.

Janis K. Fraser
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 27 October 2008 appealing from the Office action mailed 27 September 2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows:

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner. The rejection of claims 10, 18, 23, and 32 under 35 U.S.C. § 112, first paragraph (written description) is withdrawn in view of Appellant's persuasive arguments indicating that the instant specification at pages 22-23 describes the locations of the domains and consensus sequences of the encoded hOCTN1 protein.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Tamai et al. Cloning and Characterization of a Novel Human pH-Dependent Organic Cation Transporter, OCTN1. FEBS Letters 419: 107-111, 1997.

Koepsell et al. Organic Cation Transporters. Rev Physiol Biochem Pharmacol 150: 36-90, 2003

Koepsell et al. The SLC22 Drug Transporter Family. Eur J Physiol 447: 666-676, 2004

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 8, 10, 11, 13, 16, 18-21, 23-25, 27, 32, and 36 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation.

Claim 8 is directed to an isolated nucleic acid encoding a polypeptide comprising the sequence of SEQ ID NO: 1. Claim 36 recites an isolated nucleic acid encoding a polypeptide consisting of the sequence of SEQ ID NO: 1. Claim 10 is directed to an isolated nucleic acid

encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 1, with up to 30 consecutive amino acid substitutions, wherein the polypeptide is a transporter of an organic cation. Claim 32 recites the nucleic acid of claim 10 wherein the sequence of the encoded polypeptide comprises the amino acid sequence of SEQ ID NO: 1, with up to 10 conservative amino acid substitutions. Claim 11 recites an isolated nucleic acid that hybridizes under stringent conditions to a probe, the sequence of the probe which consists of the complement of SEQ ID NO: 2. Claims 16, 18-21, 23-25, and 27 recite vectors, cultured host cells, and a method of producing a polypeptide.

The specification discloses that a fetal gene library is screened and an unknown gene showing significant homology to organic cation transporters is discovered (pg 4, lines 22-30). The putative transporter, termed OCTN1, is strongly expressed in kidney, bone marrow, trachea, and fetal liver and weakly detected in skeletal muscle, lung, placenta, prostate, spleen, spinal cord, and fetal kidney and lung (pg 24, lines 1-18; Figure 2). The specification also discloses that OCTN1 is expressed in several tumor cell lines (pg 24, lines 18-21). The specification teaches that OCTN1 transports TEA, carnitine, mepyramine, quinidine, actinomycin D, etoposide, vinblastine, daunomycin (pg 18, lines 1-19; Figures 5-11). Additionally, relevant post-filing date art only teaches that OCTN1 is a polyspecific transporter that has a preference for organic cations (Koepsell et al. Rev Physiol Biochem Pharmacol 150: 36-90, 2003, especially pg 67; Koepsell et al. Eur J Physiol 447: 666-676, 2004, especially pg 671). However, the instant specification and the post-filing date art do not teach any physiological significance or functional characteristics of the OCTN1 polynucleotide (SEQ ID NO: 2) or polypeptide (SEQ ID NO: 1). The specification also does not disclose any methods or working examples that indicate

the polynucleotides and polypeptide of the instant invention are involved in any specific activity. There is no biological activity, phenotype, disease or condition, binding partner, or any other specific feature that is disclosed as being associated with OCTN1. Without any information as to the specific properties of OCTN1, the mere identification of the polypeptide is not sufficient to impart any particular utility to the claimed polynucleotides. Since significant further research would be required of the skilled artisan to determine how the claimed polynucleotide and polypeptide are involved in any activities, the asserted utilities are not substantial. Since the utility is not presented in mature form and significant further research is required, the utility is not substantial. The specification asserts the following as patentable utilities for the claimed putative OCTN1 nucleic acid (SEQ ID NO: 2):

1) to design drugs that would improve transport and absorbability mediated by the transporter (pg 14, lines 18-24).

2) for gene therapy (pg 15, lines 14-31; pg 16, lines 1-4)

3) to develop carcinostatics that would be readily absorbed by the transporter (pg 16, lines 14-16)

4) to design an antisense DNA oligonucleotide (claim 15)

Each of these shall be addressed in turn.

1) to design drugs that would improve transport and absorbability mediated by the transporter. This asserted utility is not specific or substantial. Such assays can be performed with any polypeptide and nucleic acid. Nothing is disclosed about how the transporter or a specific function of the transporter is affected by the drugs. Additionally, the specification discloses nothing specific or substantial for the drugs designed in this method. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

2) for gene therapy. This asserted utility is not specific or substantial. Such can be performed for any nucleic acid. Further, the specification does not disclose diseases associated with a mutated, deleted, or translocated OCTN1 gene (SEQ ID NO: 2). Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

3) to develop carcinostatics that would be readily absorbed by the transporter. This asserted utility is not specific or substantial. Such assays can be performed with any polypeptide and nucleic acid. Nothing is disclosed about how the transporter or a specific function of the transporter is affected by the carcinostatics. Additionally, the specification discloses nothing specific or substantial for the carcinostatics developed in this method. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

4) to design an antisense DNA oligonucleotide. This asserted utility is not specific or substantial. Antisense oligonucleotides can be designed from any polynucleotide sequence. Further, the specification does not disclose a specific DNA target. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

It is clear from the instant specification that the OCTN1 transporter polypeptide described therein is what is termed an "orphan protein" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete

characterization, this DNA and protein, may be found to have a specific and substantial asserted utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

2. Claims 8, 10, 11, 13, 16, 18-21, 23-25, 27, 32, and 36 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(10) Response to Argument

35 U.S.C. § 101 (Utility)

At the middle of page 5 of the Brief, Appellant argues that carcinostatic compounds that are identified in a screen with hOCTN1 transporter protein have the specific and substantial use of being carcinostatic compounds (i.e., able to inhibit the growth of cancerous cells). Appellant also argues that no explanation is provided as to why anyone would wish to perform such an assay with "any" polypeptide. Appellant indicates that the asserted utility is narrow and specific to the particular activity identified by Appellant for the presently claimed nucleic acids: transport of organic cations, including carcinostatic compounds. Appellant points out that hOCTN1 is able to transport organic cations, including some that are carcinostatic (Examples 6, 7). Appellant asserts that because of this demonstrated activity, the presently claimed nucleic acids, vector, and cells are useful in screening assays designed to develop new drugs that can be transported by hOCTN1 (page 31, lines 5-16; page 35, lines 6-12). Appellant's arguments have been fully considered but are not found to be persuasive. Although the specification of the instant application teaches that the hOCTN1 polypeptide transports organic cations, the instant specification does not teach any physiological significance or functional characteristics of the OCTN1 polynucleotide (SEQ ID NO: 2) or polypeptide (SEQ ID NO: 1). The specification also does not disclose any methods or working examples that indicate the polynucleotides and polypeptides of the instant invention are involved in any specific activity. There is no biological activity, phenotype, disease or condition (i.e., cancer), binding partner, or any other specific feature that is disclosed as being associated with OCTN1. The post-filing date study of Tamai et al. (FEBS Letters 419 : 107-111, 1997), co-authored by the inventors of the instant application

and disclosing an isolated nucleic acid encoding the organic transporter protein comprising the amino acid sequence of SEQ ID NO: 1 of the instant application, states that OCTN1 "was found in several human cancer cell lines as well as in normal kidney, bone marrow and trachea, although its physiological role in these tissues remains to be established. Further studies, including subcellular localization using antibody and elucidation of the mechanism of the pH dependence and metabolic energy-sensitive activity, as well as the substrate specificity, are needed to establish the physiological importance of this transporter" (page 111, column 2, last paragraph). Thus, without a specific biological activity or nexus to a disease, why would one skilled in the art want to screen for carcinostatic compounds transported by hOCTN1? Why would one skilled in the art want to develop new drugs that can be transported by hOCTN1? The proposed uses of the hOCTN1 nucleic acids and encoded polypeptides are simply starting points for further research and investigation into potential practical uses of the nucleic acids and polypeptides. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ 689 at 696.

At the bottom of page 6, regarding a specific utility, Appellant submits that the specification clearly and extensively characterizes the structural features and biological activity of the newly discovered OCTN1 gene family. Appellant states that the specification establishes that this new gene family belongs to the general class of organic cation transporters, several of which were already known and studied. Appellant's arguments have been fully considered but are not found to be persuasive. It is noted that the credibility of the claimed nucleic acid molecules has not been questioned by the Examiner, but rather, the asserted utilities are not

specific or substantial. It is also clear from the instant specification that the OCTN1 transporter polypeptide described therein is what is termed an "orphan protein" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins, namely OCT1 and OCT2. Tamai et al. (FEBS Lett 419: 107-111, 1997) indicate that the instant human OCTN1 amino acid sequence is *only* 32% similar to rat OCT1, 33% similar to rat OCT2, 31% similar to human OCT1, and 33% similar to human OCT2 (page 109, column 1, 1st full paragraph). However, organic cation transporters have a multitude of different substrates and are located in different tissues (see Koepsell et al. Rev Physiol Biochem Pharmacol 150: 36-90, 2003;; Table 1, pages 39; Table 2, page 46; Table 3, pages 49-52). Koepsell et al. even teaches that organic cation transporters (i.e., OCT1, OCT2) "are involved in a variety of physiological and pathophysiological processes" (page 65, 1st full paragraph; page 43-44). For example, OCT2 mediates the first step in hepatic or renal excretion of cationic and amphiphilic drugs while OCT3 may mediate the cellular release of acetylcholine from the placenta during nonneuronal cholinergic regulation (Koepsell Rev Physiol Biochem Pharmacol 150: 36-90, 2003; page 65, 1st full paragraph). There is little doubt that, after complete characterization, this hOCTN1 DNA and protein, may be found to have a specific and substantial asserted utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

At page 7 of the Brief, Appellant argues that the specification asserts a utility for the claimed isolated nucleic acids, namely, expressing the encoded hOCTN1 transporter proteins in cells and screening for carcinostatics that are absorbed and transported by hOCTN1. Appellant indicates that the screen permits the selection of carcinostatics that will preferentially be

absorbed by target tissues or cells that express the hOCTN1 transporter. Appellant hypothesizes that if one is trying to treat a cancer in which the cancerous cells express the hOCTN1 transporter, one can use the screen to determine whether a given known carcinostatic compound would be effectively taken up by those cells. Appellant also states that the screen can be used to identify new carcinostatic compounds that are preferentially absorbed and transported by hOCTN1, so are potentially useful for the same purpose. Appellant argues that the specification illustrates this utility by showing that hOCTN1 actually transports known carcinostatins such as actinomycin D, etoposide, vinblastine and daunomycin. Appellant's arguments have been fully considered but are not found to be persuasive. Although the specification of the instant application teaches that the hOCTN1 polypeptide transports organic cations, the specification does not teach any physiological significance or functional characteristics of the OCTN1 polynucleotide (SEQ ID NO: 2) or polypeptide (SEQ ID NO: 1). The specification also does not disclose any methods or working examples that indicate the polynucleotides and polypeptides of the instant invention are involved in any specific activity. There is no biological activity, phenotype, disease or condition, binding partner, or any other specific feature that is disclosed as being associated with OCTN1. The specification of the instant application teaches that hOCTN1 is widely expressed, with strong expression in fetal liver and adult kidney, bone marrow, and trachea. Expression is weaker in fetal kidney and lung and adult skeletal muscle, lung placenta, prostate, spleen, and spinal cord (page 24, lines 1-21). The specification only teaches that hOCTN1 is present in a few cancer cell lines, such as HeLa S3, K562, SW480, and A549 (page 24, lines 1-21). There is no evidence in the specification or the prior or post-filing art indicating that hOCTN1 is associated with or has altered expression in cancer cells isolated from tissue as

compared to a normal control. In other words, no primary tumor expression of hOCTN1 has been demonstrated. Appellant's asserted utility of utilizing hOCTN1 in a carcinostatic screening assay to identify new carcinostatic compounds that are absorbed and transported by hOCTN1 and to determine whether a carcinostatic compound would be taken up by cancer cells expressing hOCTN1 is not specific or substantial. Such assays can be performed with any polypeptide. The specification discloses nothing specific or substantial for the compounds identified in this method. Also, the specification does not disclose any specific cell types that hOCTN1 is expressed in or that hOCTN1 is associated with cancer. Significant further experimentation would be required of the skilled artisan to determine this nexus. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ 689 at 696. Although the hOCTN1 protein of the instant application is able to transport carcinostatics, the physiological function of the protein has yet to be determined. The post-filing date study of Tamai et al. (FEBS Letters 419 : 107-111, 1997), co-authored by the inventors of the instant application, discloses an isolated nucleic acid encoding the organic transporter protein comprising the amino acid sequence of SEQ ID NO: 1 of the instant application. The reference states that OCTN1 "was found in several human cancer cell lines as well as in normal kidney, bone marrow and trachea, although its physiological role in these tissues remains to be established. Further studies, including subcellular localization using antibody and elucidation of the mechanism of the pH dependence and metabolic energy-sensitive activity, as well as the substrate specificity, are needed to establish the physiological importance

of this transporter" (page 111, column 2, last paragraph). Hence, although OCTN1 may transport various organic cations, its physiological role remains to be elucidated.

At the top of page 8 of the Brief, Appellant submits that the specification clearly meets the standard of providing a substantial utility. Appellant argues that the specification teaches how the encoded proteins can be used to study the transport of various organic cations, including carcinostatic agents, in cells, and can therefore be used to screen for compounds that are amenable to being transported by these proteins. Appellant adds that the screening assays further find use in developing particular carcinostatic agents for treatment of different types of cancer, based on the expression of hOCTN1 in various tumor cell lines. No further research is necessary to confirm Appellant's identification and characterization of this gene as encoding organic cation transporter proteins, and indeed the Examiner does not challenge Appellant's characterization of hOCTN1 as an organic cation transporter. Appellant concludes that the asserted utility is substantial because it provides a significant, currently available, real-world benefit: an assay for finding the best cancer treatment for a cell or tissue that expresses the hOCTN1 transporter. The assay can select for the best treatment for a given patient's cancer from among several known carcinostatics, or can be used to find new carcinostatics. Appellant emphasizes that there is no need to know anything more about the physiological role of hOCTN1 in order for the gene to be employed as disclosed. Appellant's arguments have been fully considered but are not found to be persuasive. The specification of the instant application discloses nothing specific or substantial for the compounds screened and developed in Appellant's asserted screening assay. Also, the specification does not disclose any specific cell types that hOCTN1 is expressed in or that hOCTN1 is associated with cancer. Significant further experimentation would be required

of the skilled artisan to determine this nexus. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial. Whereas a scale or a microarray or a gas chromatograph has patentable utility as a research tool, the objects being evaluated with those research tools do not necessarily have patentable utility. In the instant case, the claimed hOCTN1 nucleic acid molecules and encoded polypeptides are not disclosed as having an activity that can be specifically useful. Thus, further research is required to identify or reasonably confirm a specific and substantial utility. MPEP §2107(I)(C) even discloses that "[l]abels such as "research tool," "intermediate" or "for research purposes" are not helpful in determining if an applicant has identified a specific and substantial utility for the invention". Such further research requirements make it clear that the asserted utility is not yet in currently available form, i.e., it is not substantial. This further experimentation is part of the act of invention and until it has been undertaken, Appellant's claimed invention is incomplete. See *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct., 1966), wherein the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

At the top of page 9 of the Brief, Appellant argues that the Office has misapplied *Brenner v. Manson,* 148 USPQ 689 (Cup. Ct. 1966) and *in re Fisher*, 421 F.3d 1365, 76 USPQ 1225 (Fed. Cir. 2005), as the facts of the present case differ from those in *Brenner* and *Fisher*.

Appellant argues that in contrast to the facts of *Brenner*, the instant specification not only describes in great detail an asserted utility for the claimed nucleic acids, but also demonstrates that this utility works. Appellant adds that the utility is not merely use in experiments to discover a possible use. Appellant submits that in contrast to *Fisher*, hOCTN1's utility is not limited to figuring out the identity and usefulness of the claimed nucleic acids. Appellant argues that the specification demonstrates hOCTN1 transports known carcinostatic organic cation compounds. Appellant points out that the asserted utility is specific because it applies to organic cation transporters, and is substantial because it is immediately applicable in a current, real-world sense: to select optimal carcinostatics for uptake by cancer cells/tissues that express the hOCTN1 transporter. Appellant's arguments have been fully considered but are not found to be persuasive. The Examiner made a *prima facie* showing that the claimed invention lacks utility and provided sufficient evidentiary basis for factual assumptions relied upon in establishing the *prima facie* showing. The Examiner cited *in re Fisher* and *Brenner v. Manson* as support for the rejection of instant claims 8, 10, 11, 13, 16, 18-21, 23-25, 27, 32, and 36 under 35 U.S.C. § 101. In fact, MPEP §2107 also relies upon *in re Fisher* and *Brenner v. Manson* when explaining the requirements for utility. Although the fact patterns of *Brenner v. Manson* and *in re Fisher* may not be identical to the fact pattern of the instant application, the case law is still applicable to the instant application because the specification does not teach any physiological significance or functional characteristics of the OCTN1 polynucleotide (SEQ ID NO: 2) or polypeptide (SEQ ID NO: 1). The specification also does not disclose any methods or working examples that indicate the polynucleotides and polypeptides of the instant invention are involved in any specific activity. There is no biological activity, phenotype, disease or condition, binding partner, or any

other specific feature that is disclosed as being associated with OCTN1. The specification of the instant application teaches that hOCTN1 is widely expressed, with strong expression in fetal liver and adult kidney, bone marrow, and trachea. Expression is weaker in fetal kidney and lung and adult skeletal muscle, lung placenta, prostate, spleen, and spinal cord (page 24, lines 1-21). The specification only teaches that hOCTN1 is present in a few cancer cell lines, such as HeLa S3, K562, SW480, and A549 (page 24, lines 1-21). There is no evidence in the specification or the prior or post-filing art indicating that hOCTN1 is associated with or has altered expression in cancer cells isolated from tissue as compared to a normal control. In other words, no primary tumor expression of hOCTN1 has been demonstrated. Appellant's asserted utility of utilizing hOCTN1 in a carcinostatic screening assay to identify new carcinostatic compounds that are absorbed and transported by hOCTN1 and to determine whether a carcinostatic compound would be taken up by cancer cells expressing hOCTN1 is not specific or substantial. Such assays can be performed with any polypeptide. The specification discloses nothing specific or substantial for the compounds identified in this method. Also, the specification does not disclose any specific cell types that hOCTN1 is expressed in or that hOCTN1 is associated with cancer. Significant further experimentation would be required of the skilled artisan to determine this nexus. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial. The Fisher court held that §101 requires a utility that is both substantial and specific. The court held that a "[p]atent application does not satisfy utility requirement of 35 U.S.C. §101 unless it discloses both "substantial" utility for claimed invention, in form of significant and presently available benefit to public, as well as "specific" utility, which is well-defined and particular benefit to public". Additionally, as

discussed previously, Appellant's further experimentation is part of the act of invention and until it has been undertaken, Appellant's claimed invention is incomplete. See *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct., 1966), wherein the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

At the bottom of page 9 through the top of page 10 of the Brief, Appellant states that the Advisory Action points out repeatedly that a biological activity (organic cation transport) is disclosed throughout the specification for hOCTN1 and that a useful screening assay that exploits that activity is disclosed and demonstrated in the Examples. Appellant contends that the Examiner dismisses the evidence of utility on the belief that the nucleic acid would not be useful by those of ordinary skill in the art unless the specification discloses what organic cations are naturally transported by the protein in vivo and/or some sort of differential expression in diseased cells versus normal cells to indicate an association of hOCTN1 with a particular disease. Appellant asserts that the Examiner has set a standard for the utility requirement that is nowhere in the law. Appellant's arguments have been fully considered but are not found to be persuasive. Contrary to Appellant's statement, the Examiner was unable to locate any statement in the Advisory Action of 01 August 2008 indicating that a biological activity (organic cation transport) is disclosed throughout the specification for hOCTN1 and that a useful screening assay that exploits that activity is disclosed and demonstrated in the Examples. The rejection of instant

claims 8, 10, 11, 13, 16, 18-21, 23-25, 27, 32, and 36 under 35 U.S.C. § 101 is in compliance with the most currently-published version of the Utility Guidelines which require that all biological inventions must have a credible, specific, and substantial ("real world" utility). Specifically, the instant specification and the post-filing date art do not teach any physiological significance or functional characteristics of the OCTN1 polynucleotide (SEQ ID NO: 2) or polypeptide (SEQ ID NO: 1). The specification also does not disclose any methods or working examples that indicate the polynucleotides and polypeptide of the instant invention are involved in any specific activity. There is no biological activity, phenotype, disease or condition, binding partner, or any other specific feature that is disclosed as being associated with OCTN1. Without any information as to the specific properties of OCTN1, the mere identification of the polypeptide is not sufficient to impart any particular utility to the claimed polynucleotides. Since significant further research would be required of the skilled artisan to determine how the claimed polynucleotide and polypeptide are involved in any activities, the asserted utilities are not substantial. Since the utility is not presented in mature form and significant further research is required, the utility is not substantial. Furthermore, the post-filing date study of Tamai et al. (FEBS Letters 419 : 107-111, 1997), co-authored by the inventors of the instant application and disclosing an isolated nucleic acid encoding the organic transporter protein comprising the amino acid sequence of SEQ ID NO: 1 of the instant application, states that OCTN1 "was found in several human cancer cell lines as well as in normal kidney, bone marrow and trachea, although its physiological role in these tissues remains to be established. Further studies, including subcellular localization using antibody and elucidation of the mechanism of the pH dependence and metabolic energy-sensitive activity, as well as the substrate specificity, are needed to

establish the physiological importance of this transporter" (page 111, column 2, last paragraph). Hence, although OCTN1 may transport various organic cations, its physiological role remains to be elucidated. Further research requirements make it clear that the asserted utility is not yet in currently available form, i.e., it is not substantial. This further experimentation is part of the act of invention and until it has been undertaken, Appellant's claimed invention is incomplete. See *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct., 1966).

At the bottom of page 10 of the Brief, Appellant uses an analogy of a compound extracted from the bark of a tree and disclosed in the specification to be useful as a starting material for synthesis of related compounds having potent anticancer activity against tumors in mammals. Appellant points out that in this hypothetical example, nothing is known about the physiological role the compound performs in the tree, nor is there any link to a known disease of the tree. Appellant concludes that there is no question that this hypothetical compound would be found to have patentable utility despite the lack of information about its physiological role. Appellant asserts that the utility of the claimed nucleic acids and encoded proteins does not hinge on knowledge of their "physiological role" nor any association with a disease. Appellant's arguments have been fully considered but are not found to be persuasive. Since the extracted compound does not have a specific biological activity or nexus to a disease (i.e., cancer), why would one skilled in the art want to use it as a starting material for synthesis of anti-cancer agents? The proposed uses of the hypothetical extracted bark compound and of the hOCTN1 nucleic acids and encoded polypeptides of the instant application are simply starting points for further research and investigation into potential practical uses of the compound, nucleic acids and polypeptides. "Congress intended that no patent be granted on a chemical compound whose

sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ 689 at 696.

At the middle of page 11 of the Brief, Appellant argues that the distinct structural features that characterized organic cation transporter proteins (Maiden et al.) and their role in drug uptake and distribution in organs were well-known (Tsuji et al., Ullrich et al., and Meijer et al.) Appellant contends that the claimed isolated nucleic acids and encoded proteins that have a well-established utility, i.e., one of ordinary skill in the art would immediately appreciate why the hOCTN1 protein is useful, based on disclosed structural and functional characteristics that establish its role as an organic cation transporter. Appellant's arguments have been fully considered but are not found to be persuasive. The Examiner acknowledges that the papers cited by Appellant provide evidence that the transport of organic cations by various transporters has been studied for more than forty years utilizing different techniques. However, simply identifying a protein as an organic cation transporter does not mean that one of skill in the art would immediately appreciate why hOCTN1 of the instant application is useful. Organic cation transporters have a multitude of different substrates and are located in different tissues (see Koepsell et al. Rev Physiol Biochem Pharmacol 150: 36-90, 2003;; Table 1, pages 39; Table 2, page 46; Table 3, pages 49-52). Koepsell et al. even teaches that organic cation transporters (i.e., OCT1, OCT2) "are involved in a variety of physiological and pathophysiological processes" (page 65, 1st full paragraph; page 43-44). For example, OCT2 mediates the first step in hepatic or renal excretion of cationic and amphiphilic drugs while OCT3 may mediate the cellular release of acetylcholine from the placenta during nonneuronal cholinergic regulation (Koepsell Rev Physiol Biochem Pharmacol 150: 36-90, 2003; page 65, 1st full paragraph). Regarding the

instant case, the post-filing date study of Tamai et al. (FEBS Letters 419 : 107-111, 1997), co-authored by the inventors of the instant application and disclosing an isolated nucleic acid encoding the organic transporter protein comprising the amino acid sequence of SEQ ID NO: 1 of the instant application, states that OCTN1 "was found in several human cancer cell lines as well as in normal kidney, bone marrow and trachea, although its physiological role in these tissues remains to be established. Further studies, including subcellular localization using antibody and elucidation of the mechanism of the pH dependence and metabolic energy-sensitive activity, as well as the substrate specificity, are needed to establish the physiological importance of this transporter" (page 111, column 2, last paragraph). Hence, although OCTN1 may transport various organic cations, its physiological role remains to be elucidated. Further research requirements make it clear that the asserted utility is not yet in currently available form, i.e., it is not substantial. This further experimentation is part of the act of invention and until it has been undertaken, Appellant's claimed invention is incomplete. See *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct., 1966).

At the middle of page 12 of the Brief, Appellant contends that SEQ ID NO: 2 could be used as a template to generate the complement of SEQ ID NO: 2, which would possess the well-established utility of being useful as a probe to detect expression of hOCTN1 in a given patient's cancer cells. Appellant argues that one could use the knowledge that hOCTN1 is or is not expressed in a patient's cancer cells to determine whether treatment with a particular organic cation carcinostatic compound would be worthwhile. Appellant submits that if hOCTN1 is found to be expressed in the cancer cells, one would then select an organic cation carcinostatic compound that had been shown (in assays disclosed in the specification) to be transported by

hOCTN1. Appellant also adds that host cells can be to express hOCTN1 polypeptide, which in turn can be used to generate antibodies specific for hOCTN1. Appellant concludes that the antibodies are useful to determine whether a given patient's cancer cells are expressing hOCTN1, and so can allow a physician to decide whether treatment with a particular organic cation carcinostatic compound known to be transported by hOCTN1 would be worthwhile. Appellant's arguments have been fully considered but are not found to be persuasive. Although Appellant indicates the nucleic acid sequence of SEQ ID NO: 2 could be used a template to generate the complement, which would possess the well-established utility of being useful as a probe, this utility is not specific or substantial. Probes can be designed from any polynucleotide sequence and the specification does not disclose specific cDNA, DNA, or RNA targets. The specification also discloses nothing about the normal levels of expression of the polynucleotide. The instant hOCTN1 gene and protein have not been associated with any diseases and disorders, such as cancer, and no physiological activity has been identified. Regarding Appellant's assertion that antibodies against hOCTN1 would be useful, antibodies can be made to any polypeptide. However, since the specification discloses nothing specific and substantial about the hOCTN1 polypeptide, both polypeptide and its antibodies have no patentable utility.

35 U.S.C. § 112, first paragraph (enablement)

At page 13 of the Brief, Appellant argues that the arguments addressing utility establish that the specification at the time of filing taught how to make and use the claimed isolated nucleic acids in assays where the encoded protein is expressed and screened for its ability to

transport a variety of organic cations, including carcinostatic compounds. Appellant also adds that the disclosure in the specification enables one of ordinary skill to use the claimed nucleic acids, vectors, and/or cells to make probes and/or antibodies that can be used to determine whether a patient's cancer cells express hOCTN1, and so could be treated with a carcinostatic agent that is transported by hOCTN1. Appellant's arguments have been fully considered but are not found to be persuasive. The Examiner believes that since Appellant has not provided evidence to demonstrate that the claimed hOCTN1 nucleic acid molecules and encoded polypeptides have a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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